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Predictive Power of Increased Heart Rate Versus Depressed Left Ventricular Ejection Fraction and Heart Rate Variability for Risk Stratification After Myocardial Infarction

Results of a Two-Year Follow-Up Study

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Objectives. **The aim of this study was to compare the predictive value of mean RR interval assessed from predischarge Holter recordings with that of heart rate variability and left ventricular ejection fraction for risk stratification after myocardial infarction.**

Background. **Heart rate variability is a powerful tool for risk stratification after myocardial infarction. Although heart rate variability is related to heart rate, little is known of the prognostic value of 24-h mean heart rate.**

Methods. **A total of 579 patients surviving the acute phase of myocardial infarction were followed up for at least 2 years. Predischarge heart rate variability, 24-h mean RR interval and left ventricular ejection fraction were analyzed.**

Results. **During the first 2 years of follow-up, there were 54 deaths, 42 of which were cardiac (26 sudden). Shorter mean RR interval was a better predictor of all-cause mortality as well as cardiac and sudden death than depressed left ventricular ejection fraction. Depressed heart rate variability predicted the risk of death better than mean RR interval for sensitivities <40%. For sensitivities ≥40%, mean RR interval was as powerful as heart rate variability. All three variables performed equally well in predicting nonsudden cardiac death. For cardiac death prediction, a left ventricular ejection fraction <35% had a 40% sensitivity, 78% specificity and 14% positive predictive accuracy; a mean RR interval <700 ms had a 45% sensitivity, 85% specificity and 20% positive predictive accuracy; and a heart rate variability <17 U had a 40% sensitivity, 86% specificity and 20% positive predictive accuracy.**

Conclusions. **Predischarge 24-h mean heart rate is a strong predictor of mortality after myocardial infarction that can compete with left ventricular ejection fraction and heart rate variability.**

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Heart rate variability is a powerful predictor of arrhythmia-related complications in patients surviving the acute phase of myocardial infarction (1,2). The predictive value of depressed heart rate variability after myocardial infarction has been shown to be independent of other risk factors, such as left ventricular ejection fraction (1), frequency of ventricular premature complexes on the 24-h Holter recording (1) and the presence of late potentials on signal-averaged electrocardiograms (ECGs) (3). It has also been demonstrated that the predictive value of heart rate variability is independent of heart rate (1,4). However, few studies have addressed the relation between heart rate and heart rate variability (5–7).

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In previous studies, heart rate assessed from standard short-term ECGs has been shown to predict mortality in postmyocardial infarction patients (8–10), as well as in the general population (11–13). However, the value of short-term heart rate in predicting mortality in postmyocardial infarction patients was low compared with other risk factors (8).

Because the predictive value of short-term heart rate variability is substantially lower than that of heart rate variability assessed from long-term recordings (14,15), it is plausible to speculate that the same might be true for mean heart rate. Thus, the aim of our study was to assess the value of mean RR interval computed from predischarge 24-h Holter recordings in predicting mortality. In a large group of postmyocardial infarction patients, the predictive value of long-term mean heart rate assessed in this way was compared with that of left ventricular ejection fraction and heart rate variability, which are well established risk factors after myocardial infarction.

Methods

Patients. The study group included 579 patients <70 years old admitted to our hospital with acute myocardial infarction

diagnosed according to previously published criteria (2), who had completed a 2-year follow-up after the index myocardial infarction. Patients were not included if they had a noncardiac disease likely to influence mortality, an important nonischemic cardiac disease, a history of cardiac surgery or permanent pacemaker insertion, or if they refused or were unable to be followed up. Patients with atrial fibrillation were excluded because this interferes with the heart rate variability analysis. Patients with bundle branch block or ventricular pre-excitation were excluded because the wide ECG patterns disturb the computer analysis of the 24-h recordings. Patients were also excluded if, for technical reasons, a 24-h Holter recording suitable for heart rate variability analysis or left ventricular ejection fraction assessment, or both, was not available. On the basis of all these criteria, a total of 224 patients were excluded and are not counted in the 579 patients of the study cohort. There was no statistically significant difference in the clinical variables of the 224 patients excluded and the 579 patients included in the study (all-cause mortality 11% vs. 9%, men 78% vs. 79%, anterior myocardial infarction 49% vs. 48%, previous myocardial infarction 18% vs. 15%, discharged with beta-adrenergic blocking agents 39% vs. 40%, thrombolytic therapy 51% vs. 54%, respectively).

During the first 2 years of follow-up, among the study cohort, there were 54 deaths (all-cause mortality), 42 of which were classified as cardiac and 26 as sudden cardiac deaths. *Sudden death* was defined as death within 1 h of the onset of new symptoms or an unexpected death during sleep (16).

Holter recording technique. Two-channel 24-h ECG recordings (modified lead III and CM_5) were obtained using either a Tracker recorder (Reynolds Medical Ltd., United Kingdom) or an 8500 Marquette recorder (Marquette Electronics). In all patients, the recordings were made at a median of 7 days (range 5 to 11) after hospital admission. A commercially available system for long-term ECG analysis (Laser Holter 8000, Marquette Electronics) was used to obtain the sequence of durations of intervals between adjacent QRS complexes of normal supraventricular configuration. Careful manual editing and visual inspection of the recording was used to ensure the quality of the RR interval data. In most of the recordings (547 out 579), all therapy, including beta-blockers, influencing heart rate and heart rate variability was terminated at least 2 days before the recording and, if applicable, restarted after the recording was completed.

Mean RR interval. The 24-h mean RR interval was calculated as the mean duration of all normal-to-normal RR intervals found on the Holter recording.

Heart rate variability. As previously described (2), heart rate variability index was calculated from each Holter recording. The frequency distribution histogram of durations of normal-to-normal RR intervals was constructed, and the value of the heart rate variability index was obtained by dividing the area of the histogram by its height. The reproducibility of heart rate variability in our department has been published previously (17).

Left ventricular ejection fraction. Left ventricular ejection fraction was determined during the initial hospital stay, at a median of 7 days (range 5 to 10) after hospital admission. In 268 patients who underwent left heart catheterization, left ventricular ejection fraction was calculated from the right anterior oblique view of the left ventricular angiogram with a Mac angiocomputer package based on the formula of Sandler and Dodge (18). In 311 patients who did not undergo left heart catheterization, radionuclide angiograms were recorded in the supine position, and the left ventricular ejection fraction was calculated by the multiple-gated method performed in the 45° left oblique projection. A previous study (3) performed in our department showed a strong correlation between ejection fraction calculated by these two methods ($r = 0.91$).

Statistical analysis. *Sensitivity* was defined as the percent of patients with a positive test result from all patients with an end-point; *specificity* as the percent of patients with a negative test result from all patients without an end-point; and *positive predictive accuracy* as the percent of patients with an end-point from all patients with a positive test result. The major end-points for analysis were all-cause mortality, cardiac death, sudden cardiac death and nonsudden cardiac death. The power of heart rate variability, mean RR interval and left ventricular ejection fraction for predicting these end-points were compared in two steps.

Step 1. The receiver operating characteristic curves, which express the dependence of specificity on sensitivity, were computed for univariate stratification (heart rate variability, mean RR interval or ejection fraction). The statistical comparison of the positive predictive characteristics was performed at selected levels of sensitivity: For a given level of sensitivity, the dichotomy limits of ejection fraction, mean RR interval and heart rate variability giving the highest positive predictive accuracy were established. Then, ejection fraction, mean RR interval and heart rate variability were compared each with each other. On the basis of the selected dichotomy limits, the subpopulation of the complete population was established for which the classification as test-positive or test-negative did not agree for the compared variables. The number of patients classified correctly by one and by the other test were compared using a standard sign-test.

Step 2. The total population was sorted according to the results of left ventricular ejection fraction, heart rate variability and mean RR interval. For each of these variables, four groups of patients were defined. There were 145 patients in the first three groups and 144 in the fourth. Each first quartile included patients with the highest values for the given variable, whereas the fourth quartile included patients with the lowest values. Comparisons of the number of end-points in individual quartiles were performed using chi-square or Fisher exact test.

To assess the relative contribution of each of the variables for risk stratification, the different groupings into quartiles were combined together. In more detail: To assess the effect of mean RR interval on risk stratification by ejection fraction, patients in each "ejection fraction" quartile were further classified according to their "mean RR interval" quartile.

Table 1. Clinical Characteristics of Patient Cohort

	Patients Without Event (n = 525)	All-Cause Mortality (n = 54)	Cardiac Death (n = 42)	Sudden Death (n = 26)	Nonsudden Death (n = 16)
Age (yr)	52.9 ± 8.8	62.8 ± 8.4	62.6 ± 8.4	61.5 ± 9.3	64.4 ± 5.2
% men	80	74	81	85	75
Anterior MI	48	52	50	54	44
Previous MI	14	26	19	15	16
Beta-blockers	43	9	10	12	6
Thombolytic agents	55	48	45	50	38

Data presented are mean value ± SD or percent of patients. MI = myocardial infarction.

Comparisons of the number of end-points in each of such subgroups were performed using again the chi-square or Fisher exact test. The same approach was repeated to assess the effect of ejection fraction on risk stratification by mean RR interval; the effect of heart rate variability on risk stratification by mean RR interval; and the effect of mean RR interval on risk stratification by heart rate variability. Because the relative values of heart rate variability and ejection fraction in risk stratification after myocardial infarction have previously been demonstrated (19), we did not investigate the combinations of these two variables.

Table 2. Values of Dichotomy Limits, Specificity and Positive Predictive Accuracy for Prediction of Cardiac Death at Different Levels of Sensitivity for Left Ventricular Ejection Fraction, Mean RR Interval and Heart Rate Variability

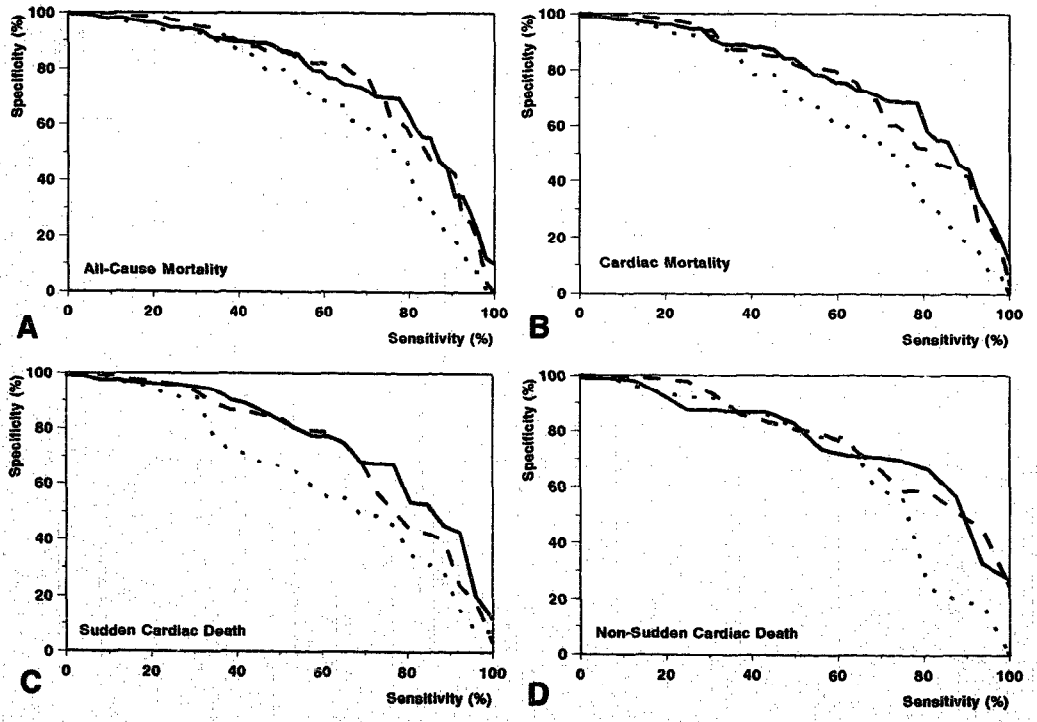
	Ejection Fraction			Mean RR Interval			Heart Rate Variability		
Sensitivity (%)	DL (%)	Spec (%)	PPA (%)	DL (ms)	Spec (%)	PPA (%)	DL (units)	Spec (%)	PPA (%)
25	26	92	23*	630	94	29	12	96	37
40	35	78	14*†	684	88	22	17	86	20
50	39	72	12*†	709	84	20	19	82	19
60	45	60	11*†	741	76	16	20	80	19
75	50	46	10*†	780	69	16	24	58	12‡

Statistical differences are marked for significantly inferior results: *$p < 0.01$ versus heart rate variability; †$p < 0.01$, ‡$p < 0.05$ versus mean RR interval. DL = dichotomy limit; PPA = positive predictive accuracy; Spec = specificity.

Results

The clinical characteristics of the study patients are shown in Table 1. The values of the dichotomy limits, specificity and positive predictive accuracy at selected levels of sensitivity for the prediction of cardiac death by all three variables are presented in Table 2. A mean RR interval <700 ms predicted cardiac death with 45% sensitivity, 85% specificity and 20% positive predictive accuracy.

Figure 1. Receiver operating characteristic curves showing the sensitivity and specificity of mean RR interval (**solid lines**), heart rate variability (**dashed lines**) and left ventricular ejection fraction (**dotted lines**) for the prediction of all-cause mortality (**A**), cardiac mortality (**B**), sudden cardiac death (**C**) and nonsudden cardiac death (**D**).



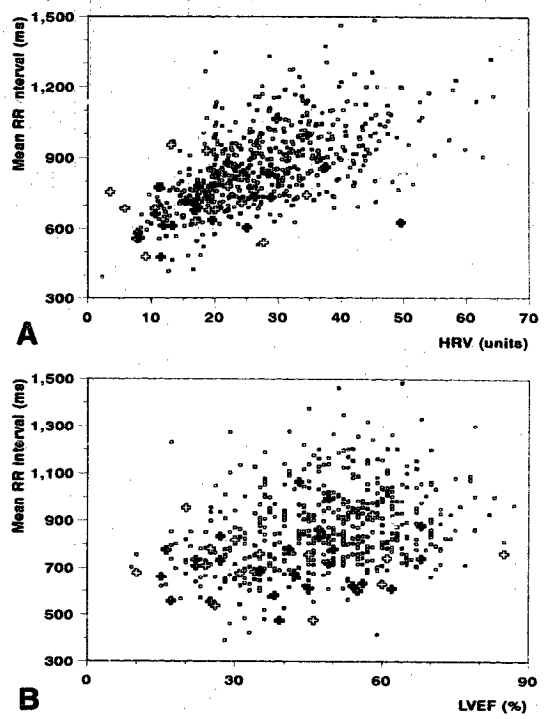


Figure 2. Scattergram showing **(A)** heart rate variability (HRV) and **(B)** left ventricular ejection fraction (LVEF) versus mean RR interval in individual patients. **Solid crosses** = sudden cardiac death; **open crosses** = nonsudden cardiac death; **dots** = patients without end-points.

The receiver operating characteristic curves displaying the relation between the sensitivity and specificity of heart rate variability, mean RR interval and left ventricular ejection fraction for predicting all-cause mortality, cardiac death, sudden death and nonsudden cardiac death are presented in Figure 1. Mean RR interval and heart rate variability performed better than ejection fraction in predicting all-cause mortality, cardiac death and sudden death. For the prediction of nonsudden cardiac death, the differences between the three variables were negligible. Only at higher sensitivity (>75%) did mean RR interval and heart rate variability appear to perform better than ejection fraction. For prediction of end-points of all categories, heart rate variability performed slightly better than mean RR interval in the low sensitivity range, whereas mean RR interval outperformed heart rate variability slightly in the high sensitivity range. These results are in agreement with the visual display of individual data shown in Figure 2.

The cutoff points for ejection fraction, heart rate variability and mean RR interval defining the different quartiles of the study cohort are presented in Table 3. The values of mean RR interval and heart rate variability were provided from Holter tapes as numbers with several decimal places, and the distinction of corresponding quartiles of the population was achieved without difficulty. However, ejection fraction values were provided rounded to the nearest percent, and many groups of patients had the same ejection fraction value. In particular, there were two sudden deaths among patients with an ejection fraction of 49%. Because the value of 49% was used as the cutoff between the second and third ejection fraction quartiles, one of these sudden death cases was classified into the second quartile and one into the third quartile.

Table 3. Definition of Quartiles for Left Ventricular Ejection Fraction, Heart Rate Variability and Mean RR Interval

Quartile	Range
$LVEF_1$ (%)	≥58
$LVEF_2$ (%)	49–58
$LVEF_3$ (%)	36–49
$LVEF_4$ (%)	≤36
HRV_1 (U)	≥34.0
HRV_2 (U)	26.2–34.0
HRV_3 (U)	20.0–26.2
HRV_4 (U)	≤20.0
Mean RR_1 (ms)	≥966
Mean RR_2 (ms)	837–964
Mean RR_3 (ms)	736–837
Mean RR_4 (ms)	≤736

Each first, second and third quartile included 145 patients; each fourth quartile included 144 patients. HRV_1 to HRV_4 = first to fourth quartiles for heart rate variability; $LVEF_1$ to $LVEF_4$ = first to fourth quartiles for left ventricular ejection fraction; Mean RR_1 to Mean RR_4 = first to fourth quartiles for mean RR interval.

Table 4 displays the percent of patients with end-points in each quartile of ejection fraction, heart rate variability and mean RR interval. Statistical differences were assessed between adjacent quartiles and between the lowest quartiles and the sum of the highest three quartiles. For all three variables (ejection fraction, heart rate variability and mean RR interval),

Table 4. Incidence of Events in Quartiles of Left Ventricular Ejection Fraction, Heart Rate Variability and Mean RR Interval Analyzed Separately

Quartile	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death
$LVEF_1$	5.5	4.8	2.1	2.8
$LVEF_2$	3.4	3.4	3.4	0
$LVEF_3$	9.0*	7.6	6.2	1.4
$LVEF_4$	19.4†‡	13.2§	6.3	6.9†§
HRV_1	3.4	2.8	2.1	0.7
HRV_2	3.4	3.4	2.8	0.7
HRV_3	6.2	5.5	2.1	3.4
HRV_4	24.3‡‖	17.4‡‖	11.1‡‖	6.3§
Mean RR_1	2.1	1.4	1.4	0
Mean RR_2	3.4	2.8	1.4	1.4
Mean RR_3	9.7*	8.3*	4.1	4.1
Mean RR_4	22.2†‡	16.7‡	11.1‡	5.6¶

*$p < 0.05$ †$p < 0.01$, ‖$p < 0.001$ versus adjacent upper quartile. ¶$p < 0.05$, §$p < 0.01$, ‡$p < 0.001$ for lowest quartile versus rest of population (i.e., sum of upper three quartiles). Results are expressed as percent of end-points in each category. Abbreviations as in Table 3.

Table 4 displays the percent of patients with end-points in each quartile of ejection fraction, heart rate variability and mean RR interval. Statistical differences were assessed between adjacent quartiles and between the lowest quartiles and the sum of the highest three quartiles. For all three variables (ejection fraction, heart rate variability and mean RR interval),

Table 5. Effect of Mean RR Interval on Risk Stratification by Left Ventricular Ejection Fraction

	Mean RR_1 + Mean RR_2 + Mean RR_3				Mean RR_4			
Quartile	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death
$LVEF_1$	4.7	3.9	1.6	2.3	12.5	12.5	6.3	6.3
$LVEF_2$	1.6	1.6	1.6	0	13.6*	13.6*	13.6*	0
$LVEF_3$	5.7	4.7	3.8	0.9	17.9*	15.4	12.8	2.6
$LVEF_4$	10.4	7.8	2.6	5.2	29.9*	19.4*	10.4	9.0

*$p < 0.05$, lowest quartile versus rest of population (i.e., sum of upper three quartiles). Results are expressed as percent of end-points in each category. Abbreviations as in Table 3.

the risk of all-cause mortality and cardiac death was statistically higher in the fourth quartile compared with the sum of first three quartiles. The same was true for sudden death for heart rate variability and mean RR interval and for nonsudden cardiac death for ejection fraction. Although the number of nonsudden cardiac deaths was not statistically different between the third and fourth quartiles for both mean RR interval and heart rate variability, there was a statistical difference between the fourth quartile and the sum of the first three quartiles for both mean RR interval and heart rate variability. The risk of sudden death was not statistically different in the four ejection fraction quartiles.

Table 5 displays the effect of mean RR interval on risk stratification by left ventricular ejection fraction. Patients in any of the lowest three quartiles for ejection fraction (quartiles 2, 3 and 4), who were also classified in the lowest quartile for mean RR interval (quartile 4) had a statistically higher risk of all-cause mortality than other patients of the same ejection fraction quartile. This was also true for cardiac death in the second and fourth quartiles for ejection fraction and for sudden death in the second quartile for ejection fraction. However, no such observation was made for nonsudden cardiac death.

The effect of ejection fraction on risk stratification by mean RR interval is shown in Table 6. For patients in the fourth quartile for mean RR interval, depressed ejection fraction (i.e., classification into the fourth quartile) significantly increased the risk of all-cause mortality. There was no other statistically significant effect of ejection fraction on risk stratification by mean RR interval.

Table 7 displays the effect of mean RR interval on risk stratification by heart rate variability. There was no effect of mean RR interval on risk stratification by heart rate variability, except for patients classified in the second heart rate variability quartile. However, within the first heart rate variability quartile, the mortality rate appeared to be higher in the fourth mean RR interval quartile (17% vs. 3%), but the difference did not reach statistical significance.

Finally, Table 8 displays the effect of heart rate variability on risk stratification by mean RR interval. Within each of the lowest two quartiles of mean RR interval, patients classified in the lowest quartile of heart rate variability were at statistically higher risk of all-cause mortality than other patients in the same mean RR interval quartile. This was also true for cardiac and nonsudden death in the second mean RR interval quartile.

Discussion

Our study suggests that, although frequently neglected, mean RR interval is a strong predictor of death after myocardial infarction. When assessed from 24-h Holter recordings, it performed better than left ventricular ejection fraction, which is a widely accepted predictor of postinfarction mortality.

Comparison with previous studies. To our knowledge, mean RR interval measured from 24-h Holter recordings has seldom been studied in postmyocardial infarction patients. In their first report on heart rate variability after myocardial infarction, Kleiger et al. (1) demonstrated that heart rate variability was an independent and better predictor of mortality than a mean RR interval <750 ms. This was further emphasized by Fleiss et al. (4) who demonstrated that mean RR interval did not predict mortality independently of the standard deviation of normal RR intervals. However, the MPIP population (8) used in those studies was different from

Table 6. Effect of Left Ventricular Ejection Fraction on Risk Stratification by Mean RR Interval

	$LVEF_1$ + $LVEF_2$ + $LVEF_3$				$LVEF_4$			
Quartile	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death
Mean RR_1	1.5	1.5	1.5	0	7.7	0	0	0
Mean RR_2	2.5	2.5	1.7	0.8	7.4	3.7	0	3.7
Mean RR_3	8.3	6.5	3.7	2.8	13.5	13.5	5.4	8.1
Mean RR_4	15.6	14.3	11.7	2.6	29.9*	19.4	9.1	9.0

*$p < 0.05$, lowest quartile versus rest of population (i.e., sum of upper three quartiles). Results are expressed as percent of end-points in each category. Abbreviations as in Table 3.

Table 7. Effect of Mean RR Interval on Risk Stratification by Heart Rate Variability

	Mean RR_1 + Mean RR_2 + Mean RR_3				Mean RR_4			
Quartile	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death
HRV_1	2.9	2.2	1.4	0.7	16.7	16.7	16.7	0
HRV_2	1.6	1.6	1.6	0	15.8*	15.8*	10.5	5.3
HRV_3	5.3	4.4	1.8	2.7	9.4	9.4	3.1	6.3
HRV_4	17.5	14.0	7.0	7.0	28.7	19.5	13.8	5.7

*$p < 0.05$, lowest quartile versus rest of population (i.e., sum of upper three quartiles). Results are expressed as percent of end-points in each category. Abbreviations as in Table 3.

that of our study. None of the patients in the MPIP study (8) received thrombolytic therapy, 21% were taking antiarrhythmic agents compared with none in our study, and 33% were treated with beta-blockers when recorded compared with 6% in our study. Moreover, only 30% of all deaths in the MPIP study were classified as sudden, whereas in our study sudden cardiac death accounted for 48% of all-cause mortality. One-year mortality was also lower in our patients (6% vs. 9%), probably because of the improvement in therapeutic care, especially the widespread use of thrombolytic agents, beta-blockers, aspirin and angiotensin-converting enzyme inhibitors. The relative increase in sudden death observed in our cohort is probably a result of the fact that patients who benefit from thrombolytic therapy may remain at risk of fatal arrhythmias as a result of a small ventricular scar but are less likely to experience progressive heart failure.

Before Holter analysis became computerized, long-term mean RR interval measurement was not readily available from Holter recordings, which were mainly used to detect ventricular ectopic beats (9). Nevertheless, several studies (8–10) demonstrated the predictive value of heart rate measured on standard ECGs for risk stratification after myocardial infarction. Heart rate was shown to predict death but not independently of other factors, such as New York Heart Association functional class, left ventricular ejection fraction or the presence of ventricular ectopic beats. The low predictive value of heart rate taken from standard ECGs may be explained by the limited amount of information provided by a short-term versus a 24-h recording. Similar differences between long- and short-term data are well known for heart rate variability (14,15).

In the general population, increased heart rate is known to be a predictor of mortality (11–13). Its predictive value was found to be independent of arterial pressure, level of cholesterol, smoking habits and age (11–13). It was also demonstrated that heart rate was a predictor not only of cardiovascular mortality, but also of all cause mortality (12). However, it was recently demonstrated (5,20) that heart rate variability was a better predictor of mortality than heart rate in two large epidemiologic studies.

Physiopathologic interpretation. It is not entirely obvious why long-term heart rate is such a strong predictor of mortality. It has been suggested (21) that heart rate has a direct effect on the development of coronary atherosclerosis. Lower heart rate results in more total time in diastole when the coronary artery flow is more steady. Because changes in the rate of flow and departures from laminar unidirectional flow may enhance atherosclerosis, it is plausible to speculate that lowering heart rate reduces atherosclerosis because it prolongs periods of stable hemodynamic patterns.

Heart rate also reflects the autonomic activity. Indeed, it has been demonstrated (22) that vagal stimulation and bradycardia increase the electrical stability of the myocardium. In our study, a shorter mean RR interval was a better predictor of sudden than of nonsudden cardiac death. This agrees with the fact that in addition to heart rate variability, a shorter mean RR interval assessed from long-term recordings might be a crude measure of overall parasympathetic withdrawal or sympathetic overdrive, or both. Compared with mean heart rate, long-term heart rate variability is probably a refined approach to the assessment of the same physiologic process and is consequently a slightly better risk stratifier after myocardial infarction.

Heart rate is also dependent on left ventricular function. Figure 2B shows that left ventricular ejection fraction at rest

Table 8. Effect of Heart Rate Variability on Risk Stratification by Mean RR Interval

	HRV_1 + HRV_2 + HRV_3				HRV_4			
Quartile	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death	All-Cause Mortality	Cardiac Death	Sudden Death	Nonsudden Death
Mean RR_1	2.1	1.4	1.4	0	0	0	0	0
Mean RR_2	2.3	1.5	1.5	0	17.3	13.3*	0	13.3†
Mean RR_3	5.6	5.6	1.9	3.7	21.6†	16.2	10.8	5.4
Mean RR_4	12.3	12.3	7.0	5.3	28.7*	19.5	13.8	5.7

*$p < 0.05$, †$p < 0.01$, lowest quartile versus rest of population (i.e., sum of upper three quartiles). Results are expressed as percent of end-points in each category. Abbreviations as in Table 3.

correlates poorly with mean RR interval. It is possible that mean RR interval measured over 24 h reflects left ventricular function during daily life. The ability of mean heart rate to be measured over long time periods could explain why it compared favorably with left ventricular ejection fraction, which is measured at rest over short time periods.

Study limitations. Our study might have been influenced by several factors. The major limitation is the number of events. Although 579 patients were followed up for 2 years, the number of end-points, especially that of nonsudden cardiac deaths, was relatively low. It is possible that left ventricular ejection fraction would have been evidenced as a more powerful predictor of nonsudden cardiac death if the end-point number was higher.

The methods we used to compare the three variables might be debated. A common way of comparing variables for risk stratification is multivariate logistic analysis (23). However, it requires determination of dichotomy values for each variable on an a priori basis. The methods we used made it possible to compare the three variables without defining their dichotomy values before the analysis.

Only three predictors of outcome were compared in this study. The study would have been more complete if clinical variables, results of exercise testing, signal-averaged electrocardiography and frequency of ectopic beats were added to the model. However, the aim of our study was to evaluate the value of heart rate compared with heart rate variability and to compare them with one of the most widely used predictors of outcome—left ventricular ejection fraction.

Conclusions. Left ventricular ejection fraction is currently a widely used risk stratifier after myocardial infarction. A depressed ejection fraction after myocardial infarction is an indication that a patient is at risk of complications and will probably benefit from a treatment with angiotensin-converting enzyme inhibitors. However, in our study both heart rate and heart rate variability were stronger predictors of mortality than ejection fraction. When 24-h Holter recording is performed after beta-blockers have been stopped, patients with a mean RR interval <700 ms are at high risk of mortality after myocardial infarction. Before the mean RR interval is widely accepted as a useful risk stratifier, further studies are needed to demonstrate that specific interventions in patients with high heart rates will decrease mortality after myocardial infarction.

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